MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral

MHRA-100741-PIP01-22

Scope of the Application

Active Substance(s)

CRISANTASPASE

Condition(s)

Treatment of acute lymphoblastic leukaemia , Treatment of lymphoblastic lymphoma

Pharmaceutical Form(s)

Solution for injection; Solution for infusion

Route(s) of Administration

INTRAMUSCULAR USE; INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Jazz Pharmaceuticals UK Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Jazz Pharmaceuticals UK Limited submitted to the licensing authority on 10/02/2023 13:29 GMT an application for a Paediatric Investigation Plan

The procedure started on 15/06/2023 11:58 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to agree a paediatric investigation plan and grant a deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100741-PIP01-22

Of 20/06/2023 16:41 BST

On the adopted decision for CRISANTASPASE (MHRA-100741-PIP01-22) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for CRISANTASPASE, Solution for injection; Solution for infusion , INTRAMUSCULAR USE; INTRAVENOUS USE .

This decision is addressed to Jazz Pharmaceuticals UK Limited, Wing B, Building 5700, Spires House John Smith Drive, Oxford Business Park South, Oxford, UNITED KINGDOM, OX4 2RW

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Condition 1: Treatment of acute lymphoblastic leukaemia (ALL) Condition 2: Treatment of lymphoblastic lymphoma (LBL)

2.2 Indication(s) targeted by the PIP:

Condition 1: Treatment of patients with ALL who have developed hypersensitivity or silent inactivation to E. coli-derived asparaginase. Condition 2: Treatment of patients with LBL who have developed hypersensitivity or silent inactivation to E. coli-derived asparaginase.

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

For both Conditions: The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

For both Conditions: Solution for injection Solution for infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable.
Non-Clinical Studies	1	(Same study for both Conditions) Study 1 (WIL-350510) A pharmacokinetic comparability study of recombinant crisantaspase and crisantaspase conjugate, administered as a single dose intravenous bolus in male CD-1 mice.
Clinical Studies	2	(Same studies for both Conditions) Study 2 (JZP458-201 Part A) Open-label, single arm multiple dose trial to confirm the dose and evaluate pharmacokinetics, safety, activity, immunogenicity of intramuscular (IM) crisantaspase in children from birth to less than 18 years of age (and adults) with ALL or lymphoblastic leukaemia (LBL) who are hypersensitive to E. coli-derived asparaginases (allergic reaction or silent inactivation). Study 3 (JZP458-201 Part B) Open-label, single arm, multiple dose trial to confirm the dose and evaluate pharmacokinetics, safety, activity, immunogenicity of intravenous (IV) crisantaspase in children from birth to less than 18 years of age (and adults) with ALL or lymphoblastic leukaemia (LBL) who are hypersensitive to E. coli-derived asparaginases (allergic reaction or silent inactivation).

Extrapolation, Modeling & Simulation Studies	1	(Same study for both Conditions) Study 4 Modelling and simulation study to evaluate the use of the product with its two formulations (IM and IV) in the proposed paediatric indication in children from birth to less than 18 years of age with ALL or lymphoblastic lymphoma (LBL) who are hypersensitive to E. coli-derived asparaginases (allergic reaction or silent inactivation).
Other Studies	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	31/12/2022
Deferral of one or more studies contained in the paediatric investigation plan:	Yes